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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/754,922	01/09/2004	Jeffrey Stavenhagen	11183-004-999 (505421-999)	8663
20583	7590	02/17/2006	EXAMINER	
JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017			TUNGATURTHI, PARITHOSH K	
			ART UNIT	PAPER NUMBER
			1643	

DATE MAILED: 02/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/754,922	STAVENHAGEN ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-83 is/are pending in the application.
 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-83 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 5-17, 19, 25, 28-30, 37-41, 67-74 in part and 1, 26, drawn to a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an Fc γ R with an altered affinity relative to a polypeptide comprising a wild-type Fc region, classified in class 530, subclass 387.1+, for example.
 - II. Claims 5-17, 19, 25, 28-30, 37-41, 67-74 in part, 2, 3, 4, 27 drawn to a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an Fc γ R11A with a greater affinity than a comparable polypeptide comprising the wild-type Fc region binds Fc γ R11A, classified in class 530, subclass 387.1+, for example.
 - III. Claims 38, 71-74 in part, 4, 18, 25, 27 drawn to a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide specifically binds Fc γ R11A with a greater affinity than a comparable polypeptide comprising the wild-type Fc region binds

Fc γ RIIIA, and said polypeptide further specifically binds Fc γ RIIB with a lower affinity than a comparable polypeptide comprising the wild-type Fc region binds Fc γ RIIB, provided that said variant Fc region does not have an alanine at any of positions 256, 298, 333, or 334, classified in class 530, subclass 387.1+, for example.

- IV. Claims 20-24 and 42-46 in part, drawn to a nucleic acid comprising a nucleotide sequence encoding a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an Fc γ R, classified in class 536, subclass 23.1, for example.
- V. Claims 20-24 and 42-46 in part, drawn to a nucleic acid comprising a nucleotide sequence encoding a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an Fc γ RIIIA, classified in class 536, subclass 23.1, for example.
- VI. Claims 31-36 in part, drawn to a method of treating cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an Fc γ RIIIA with a greater

affinity than a comparable polypeptide comprising the wild-type Fc region binds FcγRIIIA, classified in class 514, subclass 2, for example.

- VII. Claims 31-36 in part, drawn to a method of treating cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide specifically binds FcγRIIIA with a greater affinity than a comparable polypeptide comprising the wild-type Fc region binds FcγRIIIA, and said polypeptide further specifically binds FcγRIIB with a lower affinity than a comparable polypeptide comprising the wild-type Fc region binds FcγRIIB, provided that said variant Fc region does not have an alanine at any of positions 256, 298, 333, or 334, classified in class 514, subclass 2, for example.
- VIII. Claims 47, 51-55, drawn to a method for producing a tetrameric FcγR complex, wherein said tetrameric complex has an enhanced affinity for an Fc region, relative to the affinity of a monomeric FcγR for the Fc region, classified in class 435, subclass 71.1+.
- IX. Claims 48-50, drawn to tetrameric FcγR complex, classified in class 530, subclass 387.1+, for example.
- X. Claims 56 and 57 in part, drawn to a method of treating or managing cancer in a patient having a cancer characterized by a cancer antigen,

said method comprising administering to said patient a therapeutically effective amount of an antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an Fc γ R with an altered affinity relative to a polypeptide comprising a wild-type Fc region, classified in class 514, subclass 2, for example.

- XI. Claims 56 and 57 in part, drawn to a method of treating or managing cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an Fc γ RIIIA with a greater affinity than a comparable polypeptide comprising the wild-type Fc region binds Fc γ RIIIA, classified in class 514, subclass 2, for example.
- XII. Claims 56 and 57 in part, drawn to a method of treating or managing cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide specifically binds Fc γ RIIIA with a greater affinity than a comparable polypeptide

comprising the wild-type Fc region binds Fc γ RIIIA, and said polypeptide further specifically binds Fc γ RIIB with a lower affinity than a comparable polypeptide comprising the wild-type Fc region binds Fc γ RIIB, provided that said variant Fc region does not have an alanine at any of positions 256, 298, 333, or 334, classified in class 514, subclass 2, for example.

XIII. Claims 58-65, drawn to a method of treating an autoimmune disorder in a patient in need thereof, said method comprising administering to said patient a therapeutically effective amount of a molecule comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild type Fc region, such that said molecule specifically binds Fc γ RIIB with a greater affinity than a comparable molecule comprising the wild type Fc region, and said molecule further specifically binds Fc γ RIIIA with a lower affinity than a comparable molecule comprising the wild type Fc region, class 514, subclass 2, for example.

XIV. Claim 66, drawn to a method of treating an infectious disease in a patient in need thereof, said method comprising administering to said patient a therapeutically effective amount of a molecule comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild type Fc region, such that said molecule specifically binds Fc γ RIIB with a greater affinity than a comparable molecule comprising the wild type Fc region, and said molecule further

specifically binds Fc γ RIIIA with a lower affinity than a comparable molecule comprising the wild type Fc region, classified in class 514, subclass 2, for example.

- XV. Claims 75 and 76, drawn to a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide specifically binds Fc γ .RIIIA with a greater affinity than a comparable polypeptide comprising the wild-type Fc region, and said polypeptide further specifically binds Fc γ .RIIB with a lower affinity than a comparable polypeptide comprising the wild type Fc region binds Fc γ .RIIB, wherein said at least one amino acid modification comprises a set of substitutions selected from the group consisting of a substitution as listed in claim 75, classified in class 530, subclass 387.1+, for example.
- XVI. Claim 78, drawn to a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution at position 255 with glutamic acid and at position 396 with leucine, classified in class 530, subclass 387.1+, for example.
- XVII. Claim 79, drawn to a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution

at position 370 with glutamic acid and at position 396 with leucine, classified in class 530, subclass 387.1+, for example.

XVIII. Claim 80, drawn to a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution at position 392 with threonine and at position 396 with leucine, classified in class 530, subclass 387.1+, for example.

XIX. Claim 81, drawn to a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution at position 221 with glutamic acid, at position 270 with glutamic acid, at position 308 with alanine, at position 311 with histidine, at position 396 with leucine, and at position 402 with aspartic acid, classified in class 530, subclass 387.1+, for example.

XX. Claim 82, drawn to a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification, wherein said at least one amino acid modification comprises substitution at position 243 with leucine, at position 305 with isoleucine, at position 378 with aspartic acid, at position 404 with serine, and at position 396 with leucine, classified in class 530, subclass 387.1+, for example.

XXI. Claim 83, drawn to a polypeptide comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification,

wherein said at least one amino acid modification comprises substitution at position 284 with methionine, at position 298 with asparagine, at position 334 with glutamic acid, at position 355 with tryptophan, and at position 416 with threonine, classified in class 530, subclass 387.1+, for example.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions of Groups I, II, III, IV, V, IX, XV, XVI, XVII, XVIII, XIX, XX and XXI represent separate and distinct products which are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects. The polynucleic acid of Group IV and V, the polypeptide product of Groups I, II, III, XV, XVI, XVII, XVIII, XIX, XX and XXI, are structurally and chemically different from each other. The polynucleotide is made by nucleic acid synthesis, while the polypeptide is made by translation of mRNA and the antibody is raised by immunization and unidentified agonists. Further, the nucleic acid molecules of Groups IV and V; and the polypeptide molecules of Groups of I, II, III, XV, XVI, XVII, XVIII, XIX, XX and XXI are different within because of their differences in their sequences, hence differing in their structure and function. Furthermore, the polynucleotide can be used for hybridization screening and the antibody can be used to immunopurify the polypeptide and the antagonist and the agonist can be used for different methods of treatment to up-regulate and down-regulate the polypeptide in a clinical setting, for example. The examination of all groups would require different

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searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus the inventions I, II, III, IV, V, XV, XVI, XVII, XVIII, XIX, XX and XXI are patentably distinct.

The inventions of Groups VI-VIII and X-XIV are materially distinct methods which differ at least in objectives, method steps, reagents and/or dosages and/or schedules used, response variables, and criteria for success. In the instant case, Group VI recites a method of treating cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an FcγRIIIA with a greater affinity than a comparable polypeptide comprising the wild-type Fc region binds FcγRIIIA, Group VII recites a method of treating cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide specifically binds FcγRIIIA with a greater affinity than a comparable polypeptide comprising the wild-type Fc region binds FcγRIIIA, and said polypeptide further specifically binds FcγRIIB with a lower affinity than a comparable polypeptide comprising the wild-type Fc region binds FcγRIIB, provided that said variant Fc region does not have an alanine at any of positions 256, 298, 333, or 334, Group VIII recites a method for producing a tetrameric FcγR complex, wherein said tetrameric

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complex has an enhanced affinity for an Fc region, relative to the affinity of a monomeric Fc γ R for the Fc region, Group X recites a method of treating or managing cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an Fc γ R with an altered affinity relative to a polypeptide comprising a wild-type Fc region, Group XI recites a method of treating or managing cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide binds an Fc γ RIIIA with a greater affinity than a comparable polypeptide comprising the wild-type Fc region binds Fc γ RIIIA, Group XII recites a method of treating or managing cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild-type Fc region, such that said polypeptide specifically binds Fc γ RIIIA with a greater affinity than a comparable polypeptide comprising the wild-type Fc region binds Fc γ RIIIA, and said polypeptide further specifically binds Fc γ RIIB with a lower affinity than a comparable polypeptide comprising the wild-type Fc region binds Fc γ RIIB, provided that said variant Fc region

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does not have an alanine at any of positions 256, 298, 333, or 334, Group XIII recites a method of treating an autoimmune disorder in a patient in need thereof, said method comprising administering to said patient a therapeutically effective amount of a molecule comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild type Fc region, such that said molecule specifically binds Fc γ RIIB with a greater affinity than a comparable molecule comprising the wild type Fc region, and said molecule further specifically binds Fc γ RIIA with a lower affinity than a comparable molecule comprising the wild type Fc region, and Group XIV recites a method of treating an infectious disease in a patient in need thereof, said method comprising administering to said patient a therapeutically effective amount of a molecule comprising a variant Fc region, wherein said variant Fc region comprises at least one amino acid modification relative to a wild type Fc region, such that said molecule specifically binds Fc γ RIIB with a greater affinity than a comparable molecule comprising the wild type Fc region, and said molecule further specifically binds Fc γ RIIA with a lower affinity than a comparable molecule comprising the wild type Fc region. Thus, each group differs in method objectives, method steps and parameters and in the reagents used. Further, each group is unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has different mode of operation. Each invention further performs this function using structurally and functionally divergent material. Moreover, the methodology and materials necessary for detection differ significantly for each of the materials. The examination of all groups would require different searches in the U.S. PATENT shoes and the scientific literature

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and would require the consideration of different patentability issues. Thus Inventions IV-IX are separate and distinct in having different method steps and different endpoints and are patentably distinct.

The inventions of Groups I, II, III, XV, XVI, XVII, XVIII, XIX, XX and XXI and the method of Groups VI-VIII and X-XIV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (i) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § 806.05(h)]. In the instant case the antibody product as claimed can be used in a materially different process such as affinity chromatography in addition to the materially different methods of Groups VI-VIII and X-XIV.

Election of species within Group XIII

3. This application contains claims directed to the following patentably distinct species of the claimed invention XIII

If group XIII is elected, the applicant is required to elect one species from the following list:

Species a) rheumatoid arthritis

Species b) psoriatic arthritis

Species c) ankylosing spondylitis

Species d) Rieter's syndrome

Species e) psoriasis

Species f) lupus erythematosus

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 58 and 60 and 64 are generic.

The species discussed above patentably distinct because of their distinct properties including the differences in their treatment and modes of administration.

4. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over

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the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, because these inventions are distinct for the reasons given above and the search required for one group is not required for another group, restriction for examination purposes as indicated is proper.

6. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to

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be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

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8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

9. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi, Ph.D.
Ph: (571) 272-8789



LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER